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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,079	10/22/2003	Luc Mercken	FRAV2002/0030 US NP	2372

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 07/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,079	MERCKEN ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *2-5 and 10-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-14* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks filed 13 April 2006 have been entered. Claims 1 – 14 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group II in the reply filed on 13 April 2006 is acknowledged. The traversal is on the ground(s) that there would not be a serious burden to examine both Groups I and II together, and that the two groups overlap in scope and thus restriction between them is improper. This is not found persuasive because the methods of Group I require that a "reporter gene" be provided. This is not required for Group II, no specific addition of nucleic acids, that is genes, is required by any of claims 6 – 9. Furthermore claims 8 and 9 both require that "at least one mammalian cell" be provided; this is not required for the method of claims 1 – 5. Groups I and II require different starting materials and thus are patentably distinct methods. Furthermore, as the different methods require different starting materials, search for one of the sets of starting materials would not be expected to reveal the novelty or non-obviousness of a method using a different set of starting materials.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 2 – 5 and 10 – 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 13 April 2006.

4. Claims 1 and 6 – 9 are under examination.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1, 6, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1 does not require any active steps and only requires a single mental step, "identifying a Src protein inhibitor". The claimed invention does not fall into any of the categories of patentable subject matter set forth in § 101. It is not a proper process as it does not require any steps. Claims 6 and 7 both depend from claim 1 but do not recite any additional steps, such as contacting a candidate compound with a cell, which appears in claim 8.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6 – 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cellular assays which measure the degree of tyrosine kinase activity, does not reasonably provide enablement for measurement of all types of Src activity as broadly claimed in claim 8, or for all modes of "identifying" therapeutic agents, which is encompassed by claims 1 and 6 - 7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In the instant case the nature of the invention, namely finding a therapeutic compound for the treatment of Alzheimer's disease, is complex. The art recognizes that Alzheimer's disease is very difficult to treat. See for example the enclosed article by Vickers (2002. Drugs Aging 19:487-494). Vickers teaches that in 2002, the time the instant invention was made, essentially all patients who have the disease succumb to its effects. The claims are very broad

because with the exception of claims 8 and 9, they read on all possible methods of "identifying" a therapeutic compound and are not limited to those methods which involve active steps such as laboratory-based assays. Claims 8 and 9 require specific steps, but allow for the measurement of "the activity of said Src protein" which is a very broad limitation. This is encompasses not only the phosphate-transferring activity of this known kinase, but includes any and all properties or functions which could be construed as "activity". Neither protein activity nor Src activity are explicitly defined in the specification, and thus the skilled artisan must consider the broadest reasonable definition of protein activity. This term appears to encompass any and all biological activities including for example the ability of the Src protein to elicit antibodies when injected into an animal. Src protein is known to have other activities beyond tyrosine phosphorylation, such as oncogenic transformation of cells; see for example Yu et al. 1995 Science 269:81-83. Src proteins also vary in their ability to perform these various roles. Yu et al. teach that when Tyr527 is changed to Phe, cSRC becomes active, although even this degree of oncogenic potency is less than that of Rous sarcoma virus v-Src (see Yu p. 83).

However what is disclosed in the specification is relatively narrow, compared to the breadth of the claims. The specification is not enabling for all methods of "identifying an agent" as broadly claimed. Claim 1 does not require any particular steps, the claimed method can be performed just by thinking about agents. Since the claim does not limit which structural elements are required for the agent, or which proteins or residues of those proteins should be prevented from being phosphorylated by Src, the specification does not provide guidance commensurate in scope with the claim such that the identification of agents that inhibit any form of Src activity will positively identify agents for treatment of Alzheimer's disease. Furthermore, the specification does not provide guidance towards or examples of all forms of Src activity, which is to be measured in claims 8 and 9. All that is disclosed is how much Src is produced, and whether A-beta levels change in the presence of PP2, a phosphotase which inhibits Src kinases (see p. 10, for example).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Maly et al. (2000. Proc Natl Acad Sci USA 97:2419 – 2424).

Maly teaches assays for identification of Src inhibitors. See for example the paragraph spanning pp. 2421 – 2422, which teaches all steps of the assay. Figure 3 of the article shows the degree of inhibition of Src kinase activity for each of 305 compounds tested. Thus as the reference teaches the only step recited in claim 1, namely identifying a Src protein inhibitor, it anticipates claim 1. While claim 1 recites "a method for identifying a therapeutic compound for the treatment of Alzheimer's disease", this is an intended use of the compound obtained by the step of identifying, and is not given patentable weight.

10. Claims 1 and 6 – 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al. (WO 02/22660, published 21 March 2002).

Tang et al. teach screening assays for a number of proteins. The proteins are identified by SEQ ID NO:, Tang's SEQ ID NO:607 is identical to applicant's SEQ ID NO:1 (see enclosed alignment). Tang teaches assays to identify compounds which decrease the activity of the protein. See Tang, p. 56, particularly the second complete paragraph which teaches that the test compounds can "be screened for ability to bind or modulate (i.e., increase or decrease) the activity of polypeptides of the invention". As the reference teaches a method of identifying inhibitors of the protein of SEQ ID NO:1, it anticipates claims 1 and 7. While claim 1 recites "a method for identifying a therapeutic compound for the treatment of Alzheimer's disease", this is an intended use of the compound obtained by the step of identifying, and is not given patentable weight. Since SEQ ID NO:1 is a human protein (specification, p. 11), it meets the limitation of claim 6.

Tang et al. also teach every element of claim 8. The reference teaches that the screening methods are to include providing cells expressing the protein (see p. 56, first complete paragraph), which is on point to claim 8, part a). The reference also teaches that "drugs are screened against such transformed cells" which can only be by contacting the drugs (i.e., the candidate compounds) with the cell, which is on point to claim 8, part b). The reference also teaches that the test compounds are to "be screened for ability to bind or modulate (i.e., increase or decrease) the activity of polypeptides of the invention", which is on point to claim 8,

part c). Thus the reference teaches every step of the method of claim 8 and anticipates the claim.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 6 – 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 02/22660, published 21 March 2002). The reasons why Tang anticipates claims 1 and 6 – 8 are set forth in the rejection under 35 USC 102 (b) above. Briefly, Tang teaches methods of identifying inhibitors of applicant's SEQ ID NO:1 and teaches every step of the method of claim 8. Tang teaches that the host cells, which can be used in the screening assay, can be of essentially any cell type. See p. 25, second complete paragraph. Tang teaches that primary tissue culture can be used (p. 26, line 2). Tang also teaches that the polypeptides of the invention are involved in nervous system disorders and compounds which modulate the proteins' activity can be used in treatment of many neurological diseases, including Alzheimer's disease. See p. 59. However Tang does not teach the screening method wherein the cells provided are a primary culture of neurons, as recited in claim 9.

It would have been obvious to one of ordinary skill in the art to perform the assay of Tang using a primary culture of neurons, with a reasonable expectation of success. The motivation to do so would be to identify drugs for treatment of neurological diseases. While claim 9 is not anticipated by Tang, this motivation flows naturally from the reference itself. Tang

teaches the assay of claim 8, guides the artisan to select primary cultures as a suitable cell type (see p. 26), and further teaches that the compounds identified in the screening assays can be used for treatment of neurological disease (p. 59). Thus the reference motivates the artisan of ordinary skill to select neurons for the assay, as those would be the most appropriate cell type to positively identify treatments for neurological diseases including Alzheimer's.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
July 6, 2006

RH

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER